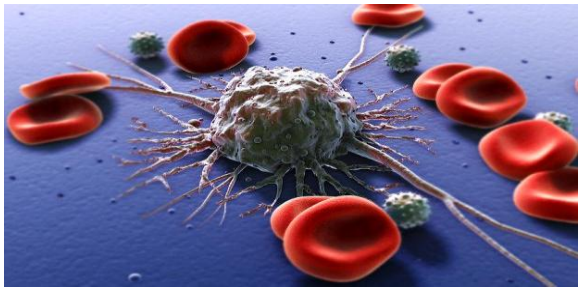

Drugs Affecting the Immune System: Antineoplastic

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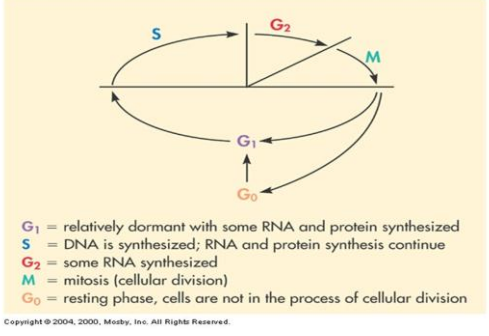
Terminology

- Oncology
  - Branch of medicine concerned with the study of malignancy – development, diagnosis, treatment, and prevention
- Antineoplastic
  - Pertaining to a substance, procedure, or measure that prevents proliferation of cells
    - Antineoplastic drugs or cytotoxic therapy are pharmaceutical agents often used to destroy cancer cells

Cell Cycle Time



Key Points

- Cancers arise from a single abnormal cell that multiplies and grows
- As abnormal cells continue to divide, they lose more of their original characteristics
  - Anaplasia — Loss of cellular differentiation & organization
  - Autonomy — Allows them to grow in an uninhibited way
  - Metastasis — Ability to travel to other sites of the body
  - Angiogenesis — Ability to grow new blood vessels to feed the tumor

Cancer chemotherapy

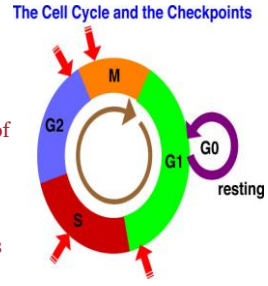
- Use of chemicals to kill cancer cells by interfering with cell replication
  - Guided by specific protocols
- Usually given in cycles
- Factors that play a major role in the response of cancer cells to anticancer drugs
  - Growth fraction
  - Doubling time
- Anticancer drugs – more effective against neoplastic cells that have high growth fraction

Antineoplastic or Anticancer Drugs

- Treat malignancies by directly killing tumor cells
  - Damage the DNA
  - Inhibit the synthesis of new DNA strands to stop the cell from replicating
  - Stop mitosis
- Destroy cancer cells by inhibiting cell division but also affect normal cells particularly the rapidly multiplying cells or cells that replace themselves quickly and causing side effects

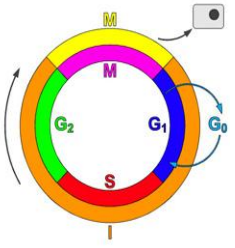
Cancer Chemotherapy

- Cell-cycle specific (CCS) agents
  - Also called "cell-cycle dependent drugs"
    - Exert their influence during a specific phase of the cell cycle
    - Most effective against rapidly growing cancer cells
    - Include: antimetabolites and mitotic inhibitors



Cancer Chemotherapy, cont.

- Cell-cycle nonspecific drugs (CCNS)
  - Also called "cell-cycle independent drug"
    - Act during any phase of the cell cycle
    - Include: alkylating drugs, anti-tumor antibiotics, hormones



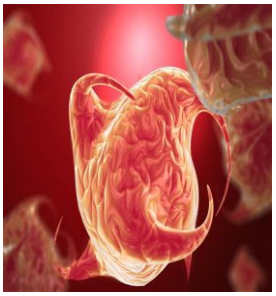
Use of Combination Chemotherapy Drugs

- Combined use of CCS & CCNS drugs maximize cell death – synergistic effect
- Able to kill cells in all phases of the cell cycle especially cells that multiply rapidly & go through the cell cycle quickly
- Decrease drug resistance and increase destruction of cancer cells
  - Example: Cyclophosphamide, Doxorubicin, & Fluorouracil are used in breast & prostate cancer

Drug Resistance

Causes of multidrug resistance (MDR)

- Cell mutation
- Natural resistance
- Gene amplification
- Ability to repair DNA damage



Specific Classes of Chemotherapy Drugs

- Alkylating agents
- Antimetabolites
- Antitumor antibiotics
- Plant alkaloids (Mitotic inhibitors)
- Miscellaneous chemotherapy agents

Alkylating Agents

- CCNS category, but most effective against cells in the G_0 phase
- Useful in the Tx of slow-growing cancers, which may have cells in the resting phase such as:
  - Lymphomas, leukemias, multiple myeloma, & solid tumors in breast, ovary, uterus, bladder, stomach
- Mechanism of action
  - Inhibit DNA synthesis by binding to and damaging the DNA itself.

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Alkylating Agents

- Pharmacokinetics
  - Degree of absorption varies
  - Metabolized and sometimes activated in the liver
  - Excreted in the urine
- Contraindications and Cautions
  - Pregnancy and lactation
  - Known allergy
  - Bone marrow suppression
  - Suppressed renal or hepatic function
- Dosing for each alkylating agent is specific for each treatment regimen

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Alkylating Agents, cont.

- Adverse effects: N/V, hemorrhagic cystitis, bone marrow suppression, alopecia, secondary malignancies, and sterility
- Major dose-limiting toxicities occur in:
  - Hematopoietic system
  - Urinary systems

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Alkylating Agents, cont.

Prototype: Cytoxan (cyclophosphamide)

- Pharmacokinetics
  - Well absorbed from GI tract
  - Moderately protein-bound
  - Metabolized in the liver
  - < 50% is excreted unchanged in the urine
- Onset of action: 2 to 3 hrs
- Therapeutic effect may take several days

Cytoxan, cont.

- Drug interaction with Cytoxan (cyclophosphamide)
  - Allopurinol or Thiazide diuretics – exaggerate the bone marrow depression
  - Phenobarbital – increases the toxicity of Cytoxan
  - Warfarin & Aspirin – potentiated effects
  - Digoxin – decreased levels
- Adverse reactions
  - Hemorrhagic cystitis - due to accumulation of toxic metabolites in the bladder
  - Secondary neoplasm
  - Bone marrow suppression

List of more alkylating drugs in textbook

Antimetabolites

- Considered to be 'S' phase specific in the cell cycle
  - Exception: Fluorouracil (5-FU, Adrucil) & floxuridine (FUDR) – considered CCNS as well as CCS
- Therapeutic actions
  - Disrupt the metabolic processes and inhibit enzyme synthesis
  - Prevent normal cellular function

Antimetabolites, cont.

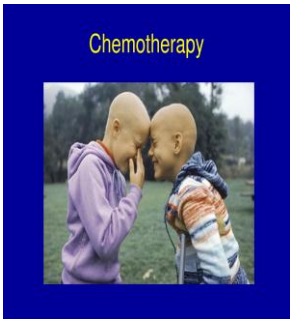
- Indications
  - Acute leukemia, breast cancer, head and neck cancer, lung cancer, osteosarcoma, non-Hodgkin's lymphoma
- Often given in combination with other agents to help overcome drug-resistant tumors

Antimetabolites, cont.

- Contraindications and cautions
  - Pregnancy and lactation
  - Known allergy
  - Bone marrow suppression
  - Renal or hepatic dysfunction
  - Known GI ulcerations or ulcerative diseases

Antimetabolites, cont.

- Adverse effects:
  - Bone marrow suppression – may lead to life-threatening infections or bleeding
  - Stomatitis, N/V/D, alopecia, rash, hepatic & renal dysfunction, & photosensitivity
  - CNS effects – headache, drowsiness, dizziness



Antimetabolites

Prototype: 5- Fluorouracil (5-FU, Adrucil)

- Action: prevention of thymidine synthetase production, thus inhibiting DNA & RNA synthesis
  - Therapeutic uses: CA of breast, cervix, colon, liver, ovary, pancreas, stomach, rectum
- Adverse reaction – similar to other antimetabolites
  - Stomatitis – an early sign of toxicity & should be reported
- Drug interactions
  - Leucovorin calcium & Metronidazole - ↑ 5-FU toxicity
  - Thiazide diuretics - ↑ myelosuppression

Antitumor Antibiotics

- Inhibit protein and RNA synthesis and bind DNA, causing fragmentation
- Classified as CCNS drugs except for bleomycin (Blenoxane) which has its major effect on the 'G_2' phase.
- Each antitumor antibiotic exhibits a unique side effect profile
  - Doxorubicin has severe cardiotoxic side effects
- Common side effects with above agents: mucositis, nausea, & vomiting

Plant Alkaloids (Mitotic Inhibitors)

- CCS and block cell division at the 'M' phase of the cell cycle
- Adverse reactions
  - Leukopenia, N/V/D, reversible alopecia
  - Damage to peripheral nerve fibers causing reversible or irreversible neurotoxicity
  - Others - loss of deep tendon reflexes, muscle weakness, joint pain, muscle weakness, bone marrow depression

Mitotic Inhibitor: Vincristine (Oncovin)

- Adverse reactions
  - hypotension, sensory loss, visual disturbances, ileus, fever, severe local reaction with extravasation, hyponatremia
- Life-threatening:
  - Intestinal necrosis, seizure, coma, acute bronchospasm, bone marrow depression
- Drug interactions:
  - Decreases the effects of digoxin and phenytoin

Miscellaneous Cytotoxic Agents

- Category includes a number of antineoplastic agents in which the mechanism of action is unclear
- Used in combination with another anticancer drug
- Examples:
  - L-asparaginase (Elspar) – used in acute lymphocytic leukemia
  - Pegaspargase (Oncaspar) - used in acute lymphoblastic leukemia
- Major toxicity – hypersensitivity reactions
- Other adverse effects – nausea, hepatotoxicity, impaired pancreatic function, coagulopathy

Hormonal Agents

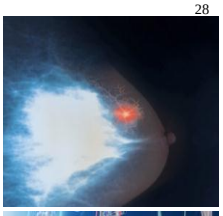
- Cytostatic – prevent the growth of the tumor instead of causing cell death
- Receptor-site specific or hormone specific to block the stimulation of growing cancer cells that are sensitive to the presence of that hormone
- Not considered biohazard agents – do not require special handling precautions
- Most are contraindicated in pregnancy
- Adverse effects – nausea, hot flashes

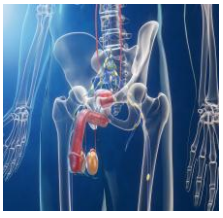
Hormonal Agents

- Corticosteroids (prednisone, dexamethasone)
  - Suppress the inflammatory process
  - Can help decrease cerebral edema caused by a malignant brain tumor
  - Some adverse effects: fluid retention, K+ loss, ↑ blood sugar, ↑ risk of infection, muscle weakness, euphoria

Hormonal Agents, cont.

- Sex hormones or hormone-like agents
  - Slow the growth of hormone-dependent tumors
  - Estrogen therapy - palliative treatment used to decrease the progression of prostate cancer in men and slow the growth of breast cancer in women
    - Examples: ethinyl estradiol (Estinyl); conjugated estrogens (Premarin)





Hormonal Agents, cont.

- Antiestrogens: tamoxifen (Nolvadex)
  - Competes with estrogen for binding sites in target tissues, such as the breast
  - Treat advance breast cancer in premenopausal women
  - Prevent tumor recurrence in both pre- and post-menopausal women
  - Adverse effects - increase risk for endometrial cancer, thrombosis, hot flashes

Hormonal Agents, cont.

- Selective estrogen receptor modulators (SERMs)
  - Act like antiestrogen but have fewer side effects
  - Examples: raloxifene (Evista)
- Progestins - may be prescribed to treat breast cancer, endometrial cancer, and renal cancer
  - Act by shrinking the cancer tissues
  - Examples: megestrol acetate (Megace), medroxyprogesterone acetate (Depo-Provera)

Hormonal Agents, cont.

- Gonadotropin-Releasing Hormone Analogues (Leutinizing hormone-releasing hormone (LH-RH) agonists) e.g. leuprolide (Lupron)
  - Suppress the secretion of follicle-stimulating hormone and luteinizing hormone from the pituitary gland
  - Results in the suppression of testosterone, preventing it from stimulating the growth of prostate cancer cells

Anticancer drugs associated with second malignancies

- Second malignancies – acute leukemias, solid tumors
- Cause toxic damage through effects on DNA, mutations, & chromosomal damage
- Long-term survivors of chemotherapy have increased risk
- Alkylating agents - drugs most commonly implicated
  - melphalan (Alkeran)
  - cyclophosphamide (Cytoxan)

Cytoprotective drugs

- Cytoprotective drugs may be used to reduce toxicities
  - IV or PO allopurinol (Zyloprim) – to reduce hyperuricemia
  - Mesna (MESNEX) – often given with high-dose cyclophosphamide (cytoxan) to inactivate urotoxic metabolites in the bladder

Serious adverse effects of Cytotoxic Drugs

- Bone marrow depression
  - 1. **Low RBC count (anemia)**
- Nursing measures
  - Assess for fatigue, SOB, VS & LOC changes, O2 sat
  - Plan rest periods for client
  - Assist with ADLs
  - Control pain, elevate HOB to facilitate breathing
  - Supplemental oxygen may be prescribed
  - Some patients may be prescribed $FeSO_4$, erythropoietin, or blood transfusion of PRBCs

Serious adverse effects, cont.

- Bone marrow depression
  - 2. **Low WBC count – leukopenia**
  - Low absolute neutrophil count (ANC) – neutropenia
  - Normal range = 1500 - 8000 cells/mm^3

    What value is considered severe? **< 500**
- Nursing measures
  - Assess for localized infections. Usual S/S of infection may be absent or greatly reduced in neutropenic patients
  - Hand hygiene
  - Visitors with infections should take precautions
  - Monitor for increase or decrease in temperature
  - Fever, chills, URTI, sore throat should be reported to HCP
  - Colony-stimulating factors, e.g., filgrastim (Neupogen) may be administered

Serious adverse effects, cont.

- Bone marrow depression
  - 3. **Low platelet count – thrombocytopenia**
- Nursing measures
  - Petechiae, bruising, bleeding gums, & nosebleeds should be reported to HCP
  - Monitor platelet counts and bleeding time
  - Assess for occult blood in urine, stool, & emesis
  - Avoid medications that may promote bleeding
  - Avoid invasive procedures
  - Apply pressure to injection sites
  - Platelet transfusions may be needed

Other serious adverse effects

- Cardiotoxicity
  - Adriamycin: May cause ECG changes or CHF
  - Cytoxan: In very high doses
  - Herceptin: Cardiomyopathy
- Nephrotoxicity

  5 –FU

  Mutamycin

Other serious adverse effects, cont.

- Hepatotoxicity:

  Cytoxan: In long term use

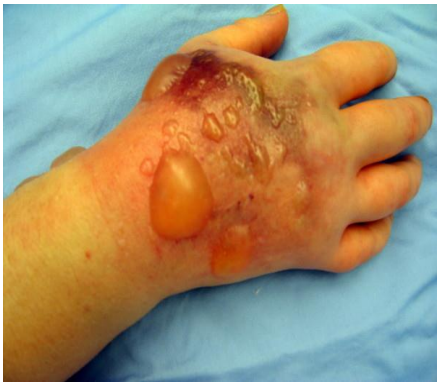
  Adriamycin: Use with caution in patients with hepatic and renal impairment

- Neurotoxicity (Peripheral Neuropathy)

Managing Complications of Chemotherapy:

A. Extravasation: escape of a vesicant drug into surrounding tissues causing severe tissue damage or permanent damage to nerves, tendons, muscles, or loss of limbs

- Usually occurs with peripheral access devices & seldom occurs when patients have central catheters
- Continuous monitoring of the IV site is critical
- Monitor for pain (may or may not be present), swelling, redness, & presence of vesicles on the skin



A. Extravasation, cont.

- If suspected, stop the IV infusion immediately but do not remove the IV line
- If possible aspirate the remaining drug or blood from the catheter
- Follow the procedure for giving the appropriate antidote according to facility policy
  - Typically given through the existing IV line or injected subQ around the infiltrated site
- Cover area with sterile, occlusive dressing if ordered
- Rest and elevate the affected extremity
- **PREVENTION** is the best approach.

B. Chemotherapy- induced nausea and vomiting (CINV)

- Among the most common and distressing symptoms experienced by clients receiving cancer treatment
- Can lead to reduction in effective drug therapy, physiologic alterations, ↓ QOL, and ↑ costs
- Antineoplastic drugs often stimulate the chemoreceptor trigger zone (CTZ) leading to N/V
- May be caused by irritation of GI tract, pain, anxiety

B. CINV, cont.

- ***Types of CINV***
  - Acute
  - Delayed
  - Anticipatory
  - Breakthrough

Table 1. Types of CINV

Type	Description
Acute	Within a few minutes to several hours of chemotherapy; ends within 24 h
Delayed	More than 24 h after chemotherapy; lasts several days (e.g., cyclophosphamide)
Anticipatory	Triggered by anything the patient associates with NV related to previous chemotherapy treatment, such as smell or taste
Breakthrough	Occurs even though preventive measures have been taken

CINV: chemotherapy-induced nausea and vomiting; NV: nausea and vomiting.
Source: References 1, 3, 5.

- Use of antiemetic agents in prophylaxis & Tx
  - **Highly emetogenic chemotherapy**:

    EXAMPLE: ondansetron (Zofran)
  - **Low- risk for emetogenic chemotherapy**

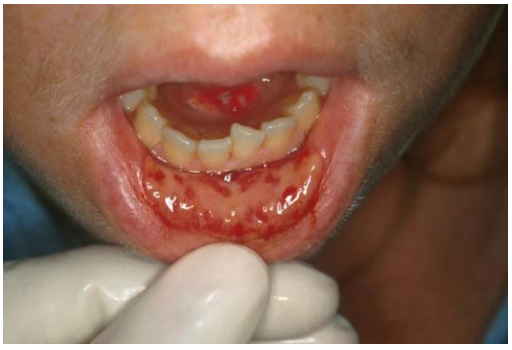
    EXAMPLE: *metoclopramide (Reglan)*, or prochlorperazine (Compazine)

- Nurse's role in preventing & managing CINV – major focus is the effective improvement of nausea & vomiting and preservation of QOL
  - Pre-treatment assessment and education
    - Patient and family expectations
    - Risk factors for CINV
    - Medication education – taking them on schedule
    - Self-care management strategies
    - Provide clear post- treatment instructions and contact numbers

  - Supportive care
    - Minimize noise, stimulation, odors
    - Frequent mouth care is needed
    - Provide flat sodas and crackers
    - Hard candies
    - Ice chips

C. *Oral Mucositis/Stomatitis*

- Ranges from mild to severe
- Therapy often begins with good oral hygiene:
  A. Avoid ETOH
  B. Avoid Mouthwashes with ETOH
  C. Avoid harsh toothpastes
  D. Soft toothbrushes or sponge toothettes



C. *Oral Mucositis/Stomatitis, cont.*

- Assess for taste changes, tissue swelling, redness, pain, dry mouth, white patches
- Symptomatic treatment may include:
  1. Mouth rinses (Maalox, Lidocaine, Benadryl mix),
  2. Antifungal medications
  3. Pain meds

- Offer ice chips or ice pops to help relieve pain
- Assess intake & output
- Evaluate caloric needs

D. Anorexia

- Loss of appetite may be related to anemia, pain, fatigue, or bitter taste caused by some chemotherapy agents
- Provide small frequent meals high in calories and protein
- Plan for rest periods
- Address issues of pain control
- Hard candy or ice chips may help relieve bitter taste

E. Diarrhea

- Diarrhea may be caused by the following:

- Other medications
- Comorbid conditions
- Enteral feedings

E. Diarrhea, cont.

- Assess normal bowel habits, monitor for F & E imbalances, I &O, and dehydration
- Antidiarrheal medications (e.g. Kaolin and Pectin)
- Small frequent meals & follow a low residue diet
- Avoid very hot or very cold foods

F. Alopecia

- Not all chemotherapeutic agents cause hair loss
- Hair thinning, patchy baldness, or complete alopecia may occur, depending on the drug
- Hair on all areas of the body is affected; hair loss may be gradual or rapid

F. Alopecia, cont.

- Hair re-growth usually occurs once therapy is completed, texture may be changed
- Before therapy: Discuss potential hair loss and ways to address the problem
- Assess for body image changes/concerns

G. Fatigue

- Can have multiple causes :
  chemotherapy, sleep disturbances, emotional distress, depression, bone marrow depression, infection, pain, or electrolyte imbalances
- Plan ways to help client conserve energy
- Plan a well-balanced diet
- Encourage clients to participate in regular but not strenuous exercise
- Encourage stress reduction measures

H. Hyperuricemia

- Increased uric acid levels due to chemotherapy-induced cell destruction
- Can cause secondary gout and obstructive uropathy
- Monitor uric acid levels
- Allopurinol (Zyloprim) may be given as a prophylactic measure
- Encourage high fluid intake

I. Infertility

- Cancer treatments can cause infertility & premature ovarian failure
- Chemotherapy, radiation, & surgery can all affect the reproductive system
- If infertility occurs it may be permanent
- Pre-treatment counseling is advised

I. *Infertility, cont.*

- Encourage clients to discuss concerns about fertility with HCP before starting cancer treatment
- Encourage clients to discuss fertility-preserving options with HCP

Guidelines for Handling Cytotoxic Drugs

- Agencies in the US most often referred to for guidelines when handling antineoplastic agents:
  - National Institute for Occupational Safety and Health (NIOSH)
  - Occupational Safety and Health Administration (OSHA)
  - Oncology Nursing Society (ONS)
  - American Society of Health-System Pharmacists (ASHP)

Guidelines for Handling Cytotoxic Drugs

- Cytotoxic drugs are potentially hazardous to personnel and patients, and appropriate waste disposal is necessary

Guidelines for Handling Cytotoxic Drugs

- Education and training on the use of supplies & equipment to reduce exposure is the cornerstone
  - Health care professionals
  - Patients & their family

Reducing Exposures

- Cytotoxic drugs can be accidentally absorbed by inhalation, contact with skin or mucous membranes, and ingestion
- Refer to agency policy and procedures
  - Most facilities mix these drugs under special environments in the pharmacy

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Reducing Exposures

- Measures to reduce exposure:
  - Wash hands
  - Prepare drugs in a separate work area
  - Avoid hand-to-mouth or hand-to-eye contact
  - Use gown, mask, glove, face shield
  - Use powder-free gloves

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Monitoring the effects of chemotherapy

- Performed at baseline, during, and after treatment
- Why monitor ?
  - To determine optimal Tx options
  - To evaluate patient response
  - To monitor toxicity

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Monitoring the effects of chemotherapy

- Five major body systems frequently monitored by laboratory tests:
  - Hematological
  - Hepatic
  - Renal
  - Cardiovascular
  - Pulmonary

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Monitoring the effects of chemotherapy

- Hematologic system – CBC, CBC with differential
  - WBC, ANC, RBC, platelet, PT, PTT
- Hepatic system – LFTs
- Renal system – creatinine, BUN, electrolytes

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Monitoring the effects of chemotherapy

- Cardiovascular system – ECG, echocardiography, cardiac enzymes
  - Anthracyclines (doxorubicin) widely known to be linked to cardiotoxicity
- Pulmonary system – PFTs
  - Bleomycin (Blenoxane) – most common cause of chemotherapy-associated pulmonary toxicity

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Nursing Implications

- Monitor for oncologic emergencies
  - Infections
  - Allergic reactions
  - Renal, liver, cardiac, and pulmonary toxicities
  - Bleeding
  - Metabolic aberrations
  - Stomatitis with severe ulcerations
  - Bowel irritability with diarrhea

Education

- Client/family/caregiver education is critical. Teaching includes:
  - Severe & often life-threatening side effects of chemotherapy drugs
  - Common complications associated with chemotherapy, how these will be managed, and when to call their HCP
  - Rectal temperature is not taken in patients who have low platelet counts
  - Safe handling and disposal of chemotherapy agents
  - Chemo drugs usually remain in the body for 48 to 72 hours after administration and is excreted in body fluids
    - Wear protective gloves when handling body fluids
    - Soiled linen from chemo spill : SPECIAL HANDLING